Original Article

Clinical Profile and Outcome in Patients of Diabetic Foot Infection

Abstract

Purpose: The aim is to study the clinical profile and outcome of patients presenting with diabetic foot infections (DFI). **Methods:** This was a prospective study recruiting patients >18 years of age, with DFI. All patients underwent a detailed history and clinical examination. Patients were classified as per the International Working Group on the Diabetic Foot -IDSA classification. The patients were followed up every month for 3 months. Clinical outcome was studied regarding the rate of amputations, readmissions, and mortality. **Results:** There were 65 patients with a mean age of 58.49 ± 11.04 years with male predilection (83.08%). Mean duration of diabetes mellitus was 12.03 ± 6.96 years. Ulcer (92.31%) and discharge (72.31%) were the most common presenting complaints. Monomicrobial growth was present in 36 patients (55.38%). Majority of isolates were Gram-negative (71.43%). The most common isolates were *Escherichia coli* and *Staphylococcus aureus* (28.57% each). Mild, moderate, and severe DFI was present in 40%, 47.69%, and 12.31% of patients, respectively. Severe DFI was associated with poor ulcer healing ($P = 0.02$) and higher number of major amputations ($P < 0.001$). Minor amputations were most commonly associated with moderate and severe DFI. Severe DFI had the highest number of readmissions ($P = 0.04$). Patients undergoing minor amputations had a significant association with area of ulcer ($P < 0.001$). **Conclusion:** This study shows the predominance of monomicrobial growth and Gram-negative organisms in diabetic foot patients. With increase in the severity of DFI, there was increased rate of hospital readmissions, amputations (major and minor), and mortality. Dimensions of ulcer may have a bearing on rate of minor amputations.

Keywords: *Amputation, diabetic foot infection, diabetic foot ulcer, diabetic foot*

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Received: 17 August, 2018.
Accepted: 03 October, 2018.

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Access this article online

Website: www.ijabmr.org

DOI: 10.4103/ijabmr.IJABMR_278_18

Quick Response Code:

Introduction

Diabetes is the leading cause of end-stage renal disease, adult-onset blindness, and nontraumatic lower extremity amputations resulting from atherosclerosis of the arteries. There were 366 million people who have diabetes worldwide in 2011, and this is expected to rise to 552 million by 2030.[1] India is the second largest contributor to the world's diabetic load after China. The complications due to diabetic foot affects >30% of the diabetic population over 40 years of age.[2]

Diabetic complications may be disabling or even life-threatening.[3] According to the International Working Group on the Diabetic Foot (IWGDF), a diabetic foot ulcer (DFU) is a full-thickness wound penetrating through the dermis (the deep vascular and collagenous inner layer of the skin) located below the ankle in a diabetic patient.[4] Eight out of 10 nontraumatic limb amputations are attributable to diabetes, of which 85% are due to DFU.[5] People with foot problems and diabetes mellitus have 15 times the increased risk of undergoing a lower extremity amputation compared to those without diabetes. The mortality after unilateral lower limb amputation has been projected to be as high as 39%–80% at 5 years, which is similar or worse than many common types of cancer.[2,5,6]

There are regional differences in the prevalence of diabetes in India varying from as low as 5.3% in Central India to as high as 13.6% in Northern India.[7] There is a scarcity of studies from North India.[7-10]

In this study, we have described the epidemiology and pattern of patients presenting with DFU and the association of clinical parameters with outcome regarding ulcer healing, number of amputations, and mortality.

Methods

This was a prospective study conducted at tertiary care institute, recruiting

How to cite this article: Seth A, Attri AK, Kataria H, Kochhar S, Seth SA, Gautam N. Clinical profile and outcome in patients of diabetic foot infection. Int J App Basic Med Res 2019;9:14-9.

patients >18 years of age with diabetic foot, attending the Diabetic foot clinic from January 2015, to May 2016. Informed consent was taken from all the patients. The study followed the Declaration of Helsinki guidelines and was approved by the Institutional Ethics Committee. The patients who had deranged renal function tests, previously undergone revascularization surgery or Burger's disease were excluded. All the patients underwent detailed history including duration of diabetes, presenting features and clinical examination at baseline including details of ulcer, evaluation of palpable pulses (i.e., femoral, popliteal, anterior tibial, posterior tibial, and dorsalis pedis) and Ankle-brachial index (ABI). The discharge from ulcer was sent for microbiological examination. Patients were classified as per the IWGDF-IDSA classification into mild, moderate, and severe diabetic foot infections (DFI).[4] Ulcer size was determined by tracing the outline of the wound on a graph paper divided into 1 cm squares. Wound area was calculated by manually counting the squares within the wound. The ulcers of the patient were debrided, antibiotic was given as per culture sensitivity, and the daily aseptic dressing was done. The patients were followed up every month for 3 months. The outcome was assessed in terms of ulcer healing, readmission, minor/major amputation, and mortality during the 3 months.

The statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS Version 20, IBM, NY, USA). Normality of the data was checked by Kolmogorov Smirnov test. The quantitative data were presented as mean ± SD For normally distributed data, means were compared using Independent *t*-test, for skewed data/scores Mann–Whitney U-test was applied. Chi-square test was applied for qualitative data. A value of $P < 0.05$ was considered statistically significant. The association of clinical outcome (ulcer healing, readmission, minor/major amputations, and mortality) with various parameters were computed using Cross tabs-Chi-square test or ANOVA. A baseline logistic regression analysis was carried out with all the parameters.

Results

Demography

There were 65 patients with the mean age of 58.49 ± 11.04 years and predilection for males ($n = 54$, 83.08%) compared to females ($n = 11$, 16.92%). A maximum number of the study patients, ($n = 29$, 44.62%), were seen in the age group of 55–64 years as tabulated in Table 1.

Diabetes profile

Mean duration of diabetes mellitus was 12.03 ± 6.96 years with mean hemoglobin A1c (HBA1c) of 7.23 ± 1.57. Majority of patients were on oral hypoglycemic agents (OHA; $n = 35$, 53.85%). Twenty-four patients (36.92%) were on insulin, and six patients (9.23%) were on combined insulin and OHA.

Presenting complaints

The ulcer was the most common presenting complaint seen in 60 (92.31%) patients. Discharge from the foot wound was the second most common presenting feature which was present in 47 (72.31%) patients. The other presenting features are depicted in Figure 1.

Clinical parameters

Palpable arteries

The femoral artery was palpated in all limbs. The popliteal artery, anterior tibial artery, posterior tibial artery, and dorsalis pedis artery was palpable in 64, 46, 40, and 38 limbs.

Ankle Brachial Index

The mean ABI was 0.58 ± 0.11.

Severity of diabetic foot infections

In total of 65 patients, most patients had moderate DFI ($n = 31$, 47.69%). Mild DFI was present in 26 patients (40%), and severe DFI was present in 8 patients (12.31%).

Spectrum of microorganisms

The microbiological profile of our patients showed that monomicrobial growth was present in 36 patients (55.38%), polymicrobial growth was present in six patients (9.23%). Among all patients, the culture was sterile in 23 patients (35.39%). Majority of isolates were Gram-negative ($n = 35$, 71.43%), whereas Gram-positive isolates were present in ($n = 14$, 28.57%).

Table 1: Age distribution of patients

Age group (years)	Number of patients (%)
15-24	1 (1.54)
25-34	2 (3.08)
35-44	1 (1.54)
45-54	14 (21.54)
55-64	29 (44.62)
65-74	14 (21.54)
≥75	4 (6.14)
Total	65 (100)

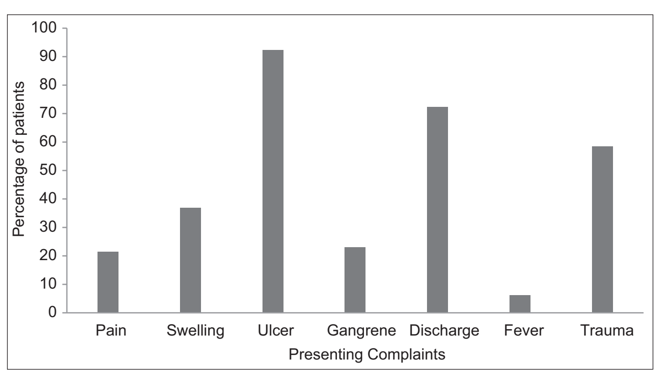

Figure 1: Complaints of patients

The most common isolates were *Escherichia coli* and *Staphylococcus aureus* (28.57% each) followed by Acinetobacter (12.24%) as depicted in Table 2.

Ulcer healing

The mean baseline area of ulcer was 14.85 cm ± 23.12 cm, mean ulcer area at 1 month was 11.75 cm ± 22.68 cm, mean ulcer area at 2 months was 8.44 cm ± 22.05 cm and mean ulcer area at 3 months was 6.38 cm ± 21.19 cm. Percentage of ulcer healing at 1 month was 20.88%, at 2 months was 43.16%, and at 3 months was 57.04% which was significant at all-time points ($P < 0.001$) [Table 3].

Follow-up

The patients were followed up every month for three consecutive months. Six patients required hospital admission at the 1st month, 4 patients were admitted at the 2nd month, whereas two patients required admission to the hospital at the 3rd month. Twenty-five (38.46%) patients underwent minor amputations, and 5 (7.69%) patients underwent major amputations. Two patients died during the follow-up.

Association of palpable arteries with clinical outcome

Ulcer healing

Ulcer healing at the 1st, 2nd and 3rd month had significant association with palpable anterior tibial artery (P = 0.04, <0.01, and <0.01, respectively), posterior tibial artery (P < 0.01 at 1st, 2nd, and 3rd month), dorsalis pedis artery (P = 0.04, <0.01, 0.01, respectively).

Table 2: Microbiological distribution

Spectrum	Number of patients (%)	Relative percentage of isolates
Gram-negative	35 (53.85)	71.43
Gram-positive	14 (21.54)	28.57
Mono-microbial	36 (55.38)	
Polymicrobial	6 (9.23)	
Sterile	23 (35.39)	
Candida	0	
Gram-negative		
Escherichia coli	14 (21.54)	28.57
Klebsiella pneumoniae	6 (9.23)	12.24
Proteus mirabilis	2 (3.08)	4.09
Acinetobacter	13 (20)	26.53
Gram-positive		
Staphylococcus aureus	14 (21.54)	28.57
MRSA	2 (3.08)	4.08
Total number of isolates	49	
Number of isolates per patient	0.75	

MRSA: Methicillin-resistant Staphylococcus aureus

Table 3: Ulcer healing during follow-up

Ulcer area (cm²)	Baseline	1 month	2 months	3 months
Mean±SD	14.85±23.12	11.75±22.68	8.44±22.05	6.38±21.19
Percentage of wound healing		20.88	43.16	57.04
P*		<0.001	<0.001	<0.001

*P<0.05 significant. SD: Standard deviation

Readmissions

The total readmissions had a significant association with palpable anterior tibial, posterior tibial artery, and dorsalis pedis (P = 0.01, 0.01, and <0.01, respectively).

Amputations

The number of both major and minor were significantly associated with palpable anterior tibial artery (P = 0.01 and <0.01, respectively), posterior tibial artery (P = 0.05 and 0.01, respectively) and dorsalis pedis artery (P = 0.01 and 0.04, respectively) while the palpable popliteal artery had a significant association with the number of minor amputations only (P = 0.04).

Mortality

Mortality had no significant association with any of palpable arteries.

Association of Ankle Brachial Index with the clinical outcome

There was a significant association of ABI with a total number of readmissions (P = 0.05). There was no association with ulcer healing, minor or major amputations, and mortality.

Association of severity of diabetic foot infections with clinical outcome

There was a significant association of severity of DFI with the rate of ulcer healing/amputations. Severe DFI was associated with poor ulcer healing and a higher number of major amputations. Minor amputations were most commonly associated with moderate and severe DFI. Similarly, patients with severe DFI had the highest number of readmissions. Table 4 shows the association between severity of DFI and ulcer healing, amputations, readmissions, and mortality.

Predictive risk factors

Logistic regression analysis was performed to see which factors could predict the risk of outcome measures. A number of patients who were readmitted to hospital at the 1st, 2nd, 3rd month or who died or underwent major amputations during the follow-up period were less for any statistical analysis. Patients undergoing minor amputations had a statistically significant association with dimensions of ulcer, i.e., area of ulcer (P = 0.00). On performing ROC plots, the cutoff value for ulcer dimension (area) was 2.13 cm² with sensitivity of 0.88 and 1-specificity of 0.37.

Discussion

Diabetic foot lesions are one of the most common causes of hospitalizations and caused by number of sociocultural

Table 4: Association of severity of diabetic foot infections with clinical outcome

Outcome	Severity of DFI				P*
	Total (n=65), n (%)	Mild (n=26; 40%), n (%)	Moderate (n=31; 47.69%), n (%)	Severe (n=8; 12.31%), n (%)	
Ulcer healing at 1st month		49.79%	28.60%	27.73%	0.03
Ulcer healing 2nd month		80.13%	68.98%	55.56%	0.03
Ulcer healing 3rd month		93.27%	83.44%	72.33%	0.02
Minor amputation	25 (38.46)	4 (15.38)	16 (51.61)	4 (50)	0.003
Major amputation	5 (7.69)	0	3 (9.68)	2 (25)	0.001
Readmission at 1st month	6 (9.23)	0	5 (16.13)	1 (12.5)	0.002
Readmission 2nd month	4 (6.15)	0	2 (6.45)	2 (25)	0.01
Readmission at 3rd month	2 (3.08)	0	1 (3.23)	1 (12.5)	0.04
Mortality	2 (3.08)	0	1 (3.23)	1 (12.5)	0.04

*P<0.05 significant. DFI: Diabetic foot infections

practices in India like barefoot walking, inadequate facilities for diabetic care, low level of education, and poor socioeconomic conditions.

The mean age in our patients was 58.49 ± 11.04 years which was similar to that previously reported in the literature.[9,10] Maximum number of patients was found in 55–64 age group (n = 29, 44.62%). It may be because that Diabetes Mellitus type II is classically seen in elderly patients, though recent reports have shown it to affect adolescent population too.[11,12] A large number of Type II patients remain asymptomatic and develop complications due to prolonged hyperglycemia, whereas Diabetes Mellitus type 1 is detected early and the affected patients donot have any complications at presentation.[13] The male preponderance for DFU reported by other studies,[10,14,15] was also seen in our study, with the disease being 5 times more common in males than females. The males high risk of developing diabetic foot complications because of increased prevalence of neuropathy, less joint mobility, and higher foot pressure.[16]

The mean duration of diabetes mellitus in our patients was 12.03 ± 6.96 years. The mean value of HbA1c observed in our study was 7.23 ± 1.57. Christman *et al*. observed that for each 1.0% point increase in HbA1c, the daily wound-area healing rate decreased by 0.028 cm^2/day.[17]

IWGDF-IDSA classification classifies the severity of DFI according to the extent of involvement and the presence of systemic inflammatory response.[4] In our study, there was a preponderance of patients with moderate DFI (49.23%) whereas severe DFI was present in 12.3% of patients. The proximal bigger arteries were more palpable than distal smaller vessels because diabetes is microangiopathy. Moreover, they are prone to tissue edema due to microvascular disease, making palpation of pulses more difficult.[18] The mean ABI in this study was 0.58 ± 0.11. Williams *et al*. observed that ABI values <0.9 indicate significant arterial disease and values >1.15 shall be regarded unreliable due to the presence of arterial calcification.[18]

In our study, monomicrobial growth was present in 55.38%, and polymicrobial growth was seen in 9.23% of patients. The cultures were sterile in 35.39% of patients. The reported proportion of monomicrobial growth in the literature varies from 63.5% to 83.5% while that of polymicrobial growth varies from 14.3% to 35%.[14,15,19,20] According to Jasmine *et al*., 20.4% had sterile cultures, whereas they were seen only in 9.8% according to a study by Bansal *et al*.[14,19] The traditional recognition that "DFI is mostly caused by S. *aureus* or Gram-positive species" may not reflect a universal clinical feature, and geographic variance emphasizes the need for local treatment guidelines. This necessity has lately been demonstrated by many studies, including the present one, and other studies from Eastern countries, which reported a significant shift toward more Gram-negative organisms isolated from DFIs.[20]

In our study, predominantly Gram-negative organisms were isolated in 35 (71.43%) patients while Gram-positive organisms were isolated in 14 (28.57%) patients. Ramakant *et al*. similarly observed that Gram-negative organisms (n = 932, 51.7%) were common than Gram-positive organisms (n = 511, 31.3%) in DFI.[10] Gadepalli *et al*. in their study on 80 ulcer specimens observed that 23 patients (28.7%) had Gram-negative and only 11 patients (13.8%) had Gram-positive infections.[9] Some studies from west reported Gram-positive organisms to be predominant organisms in DFI.[21-23] The difference observed in the prevalence of Gram-negative bacilli in DFI between diabetic patients from eastern and western countries remains largely unknown. However, environmental factors such as sanitary habits, for example, use of water for perianal wash (ablution) after defecation leading to contamination of hands with fecal flora, could be responsible for increased Gram-negative infections in the developing world compared with the West.[20]

Our culture revealed that most common isolates were *E. coli* (21.54%), *Acinetobacter (20%), Klebsiella pneu*monia (9.23%), and *Proteus Mirabilis* (3.08%) among the Gram-negative organisms. A similar finding was reported by Jog *et al*. which showed 37.7% of *E. coli*, 12.6% of *K. pneumoniae* and 7.93% of *Proteus* species among Gram-negative isolates.[24] Another study from North India reported pseudomonas to be most common isolate from bone and soft tissue (26.9 and 23.2%, respectively) followed by Acinetobacter in DFUs. They hypothesized that infection in DFU is usually polymicrobial due to chronic nature but when inadequately treated with antimicrobials, the sensitive organisms such as *E. coli*, Proteus are killed, leading to preponderance of monomicrobial growth and multidrug-resistant organisms like Pseudomonas.[8]

In our study, among Gram-positive organisms, *S. aureus* was the most common isolate which was present in 14 (21.54%) of the patients. Gadepalli *et al*. also observed that *S. aureus* was the most frequent organism isolated in DFI, being present in 13.7% of patients.[9]

Association of clinical parameters with outcome

Though detection of foot pulses is more difficult in patients with diabetes, in our study, we found a significant association of palpable infrapopliteal arteries with total number of readmissions, minor/major amputations and ulcer healing at 1st, 2nd and 3rd month. This suggests that the presence of palpable infrapopliteal arteries (anterior tibial, posterior tibial and dorsalis pedis artery) was clinically associated with favorable outcomes regarding ulcer healing and a lesser number of readmissions and amputations.

ABI did not show any association with outcome, i.e., minor and major amputations, ulcer healing or mortality in our study, but it showed a borderline significance with a total number of readmissions ($P = 0.05$). Although ABI is highly predictor of arterial occlusive disease, long-standing diabetes mellitus causes calcification of media of the vessels resulting in high systolic pressure in the ankle making it less reliable in the diabetic foot patients.[25]

Nearly 39% of our patients underwent minor amputations, and 7.69% patients underwent major amputations while two patients died during the follow-up. The mortality rate, rate of major and minor amputation increased with the increase in the severity of DFI. Though there was significant ulcer healing at all follow-up visits with appropriate antibiotic therapy, poor ulcer healing was seen with increasing severity of DFI. Therefore, the Infectious Diseases Society of America-(IDSA-IWGDF) system is clinically helpful in predicting outcomes in patients of DFI. Lavery *et al*. conducted a prospective study to validate IDSA-IWGDF system to predict outcome in DFI. They observed that there was a trend toward an increased risk of amputation, higher level amputation, and lower extremity-related hospitalization with increasing infection severity. It supports the clinical value of the IDSA-IWGDF diabetic foot classification in predicting clinical outcomes.[26] According to Wukich *et al*. 55% of patients with a severe DFI required some amputation as compared to 42% of patients with a moderate DFI.[27]

Patients undergoing minor amputations had a significant association with dimensions of the ulcer. On ROC plots, the ulcer area of 2.13 cm^2 had a sensitivity of 88%. This might suggest that the dimensions of ulcer can be a good screening tool to predict the unfavorable outcome regarding minor amputations.

Conclusion

The small sample size is the limitation of this study. To conclude, the risk of DFU occurs during the late 5th and early 6th decades of life and is common in male patients. There was a predominance of monomicrobial growth and Gram-negative organisms. Delayed ulcer healing, amputations (major and minor), hospital readmissions and mortality increased with increasing severity of DFI. Minor amputation was seen in more than one-third of patients with DFU. The higher number of minor and major amputations poses burden on existing healthcare and human resources of the country. Increase in dimensions of ulcer has a bearing on the rate of minor amputations. Hence, healthcare education and screening programs should be strengthened especially in developing nations, to prevent DFI. Healthcare should be made more accessible, to facilitate early diagnosis of DFI and its complications, to minimize the rate of amputations.

Acknowledgment

The authors would like to thank Dr. Natasha Gautam Seth for her contribution in data analysis.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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